L1 L2	FILE 'REGISTRY' ENTERED AT 14:01:17 ON 26 JAN 2010  EXP 1/(2-CYANO-2-DEOXY-/CN  EXP 1-(2-CYANO-2-DEOXY-/CN  EXP 1-(2-C-CYANO-2-DEOXY-/CN  STRUCTURE UPLOADED  3 S L1
	FILE 'STNGUIDE' ENTERED AT 14:08:01 ON 26 JAN 2010
L3 L4 L5	FILE 'REGISTRY' ENTERED AT 14:09:43 ON 26 JAN 2010 STRUCTURE UPLOADED 3 S L3 67 S L3 SSS FULL
L6 L7 L8 L9	FILE 'HCAPLUS' ENTERED AT 14:10:49 ON 26 JAN 2010 61 S L5/THU 974388 S CANCER OR TUMOR OR NEOPLA? 49 S L6 AND L7 22 S L8 AND (PY<2004 OR AY<2004 OR PRY<2004)
L10	FILE 'REGISTRY' ENTERED AT 14:11:53 ON 26 JAN 2010  EXP ROSCOVITINE/CN  1 S E2-E3
L11 L12 L13 L14 L15 L16	

```
=> file registry
COST IN U.S. DOLLARS
```

FULL ESTIMATED COST

SINCE FILE TOTAL
ENTRY SESSION
0.22 0.22

FILE 'REGISTRY' ENTERED AT 14:01:17 ON 26 JAN 2010 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2010 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 JAN 2010 HIGHEST RN 1203540-14-0 DICTIONARY FILE UPDATES: 25 JAN 2010 HIGHEST RN 1203540-14-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

```
=> \exp 1/(2-cyano-2-deoxy-/cn
            1 1E-HYDROXYTESTOSTERONE/CN
E1
E2
             1
                  1E-HYDROXYURSODEOXYCHOLIC ACID/CN
            0 --> 1/(2-CYANO-2-DEOXY-/CN
Е3
            1 1/2MO/CN
1 1/2PACM/CN
1 1/4CR-1MO/CN
1 1/4NC(LIG)/CN
1 1/8BNC/CN
E4
E5
Ε6
Ε7
            1
                 10 20 XFC/CN
                 10 CADHERIN (DANIO RERIO GENE CDH10)/CN
E10
            1
E11
            1
                  10 CADHERIN (DANIO RERIO GENE PCDH10)/CN
E12
             1
                  10 CARAT/CN
=> \exp 1-(2-cyano-2-deoxy-/cn
E1
                   1-(2-CYANO-1-METHYLETHYL)-2-ISOPROPYLIMIDAZOLE/CN
             1
                   1-(2-CYANO-1-METHYLETHYL)-2-ISOPROPYLIMIDAZOLE MONOPICRATE/C
E_2
             1
                   Ν
E.3
             0 \longrightarrow 1-(2-CYANO-2-DEOXY-/CN
E4
             1
                   1-(2-CYANO-2-METHYLPROPYL)-3-(2-FLUORO-4-((PIPERAZIN-1-YL)CA
                   RBONYL) PHENYL) UREA/CN
E5
             1
                   1-(2-CYANO-3'-METHYLBIPHENYL-4-YL)-1H-PYRAZOLE-4-CARBOXYLIC
                   ACID/CN
                   1-(2-CYANO-3'-METHYLBIPHENYL-4-YL)-1H-PYRAZOLE-4-CARBOXYLIC
E6
             1
                   ACID ETHYL ESTER/CN
             1
E7
                   1-(2-CYANO-3,4-DIMETHOXYPHENYL)-3-BUTYLUREA/CN
Ε8
             1
                   1-(2-CYANO-3, 4-DIMETHOXYPHENYL)-3-METHYLUREA/CN
E9
             1
                  1-(2-CYANO-3-METHYLPHENOXY)-2,3-EPOXYPROPANE/CN
             1
E10
                  1-(2-CYANO-3-METHYLPHENOXY)-2-HYDROXY-3-ISOPROPYLAMINOPROPAN
                  E HYDROCHLORIDE/CN
                  1-(2-CYANO-3-METHYLPHENOXY)-2-HYDROXY-3-TERT-BUTYLAMINOPROPA
E11
    1
```

NE-HYDROCHLORIDE/CN E12 1-(2-CYANO-3-PYRAZINYL)-4-(3-(6-METHYL-2-PYRIDYL)-2-PROPYNYL1 IDENE) PIPERIDINE/CN  $=> \exp 1-(2-C-cyano-2-deoxy-/cn$ 1-(2-BUTYRYLOXYETHOXY)ETHYL METHACRYLATE/CN 1 E2 1 1-(2-C-ALLYL-B-D-RIBOFURANOSYL) THYMINE/CN Е3  $0 \longrightarrow 1-(2-C-CYANO-2-DEOXY-/CN$ E41 1-(2-CARBAMOYL-1-METHYLETHYL)-1-METHYLPYRROLIDINIUM IODIDE/C E5 1 1-(2-CARBAMOYL-1-METHYLETHYL)PYRIDINIUM BROMIDE/CN 1-(2-CARBAMOYL-1-METHYLETHYL)PYRIDINIUM CHLORIDE/CN Ε6 1 E7 1-(2-CARBAMOYL-1-METHYLETHYL)PYRIDINIUM IODIDE/CN 1 E8 1 1-(2-CARBAMOYL-4-(6-FLUORO-7-(METHYLAMINO)-4-OXO-2H-BENZO(E)(1,3) OXAZIN-3 (4H) -YL) PHENYL) -3- ((5-CHLOROTHIOPHEN-2-YL) SULFO NYL) UREA/CN 1-(2-CARBAMOYLETHYL)-1-METHYLPIPERIDINIUM BROMIDE/CN E9 1 1-(2-CARBAMOYLETHYL)-1-PYRIDINIUM METHANESULFONATE/CN E10 1 1-(2-CARBAMOYLETHYL)-2-(P-DIETHYLAMINOPHENYL)BENZ(CD)INDOLIU E11 1 M CHLORIDE/CN E12 1 1-(2-CARBAMOYLETHYL)-2-METHYLPYRIDINIUM PICRATE/CN => log hold COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 0.49 0.71

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 14:02:04 ON 26 JAN 2010

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:SSPTAEXO1623

## PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \* \* SESSION RESUMED IN FILE 'REGISTRY' AT 14:07:09 ON 26 JAN 2010 FILE 'REGISTRY' ENTERED AT 14:07:09 ON 26 JAN 2010 COPYRIGHT (C) 2010 American Chemical Society (ACS)

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION 0.49 0.71

=>

Uploading C:\Program Files\STNEXP\Queries\10581585nucleoside.str

```
chain nodes :
8  9  16  17  18  19  20  21  22  23  26  28  29  30  31  32  33  34  35  36
ring nodes :
3  4  5  6  7  10  11  12  13  14  15
chain bonds :
3-19  3-31  4-20  4-30  6-10  6-34  7-8  7-33  8-9  11-17  13-16  14-36  15-35
16-18
16-26  19-32  20-28  21-22  21-23  28-29
ring bonds :
3-4  3-7  4-5  5-6  6-7  10-11  10-15  11-12  12-13  13-14  14-15
exact/norm bonds :
3-4  3-7  3-19  4-5  5-6  6-7  6-10  8-9  10-11  10-15  11-12  11-17  12-13  13-14
13-16  14-15  16-26  21-22  21-23
exact bonds :
3-31  4-20  4-30  6-34  7-8  7-33  14-36  15-35  16-18  19-32  20-28  28-29
```

G1:0,NH

G2:0,S

## G3:H, [\*1]

Connectivity:

23:1 X maximum RC ring/chain

Match level:

3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom 12:Atom

13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS

21:CLASS 22:CLASS

23:CLASS 26:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS

34:CLASS 35:CLASS

36:CLASS

Generic attributes :

23:

Saturation : Saturated Number of Carbon Atoms : 7 or more

#### L1 STRUCTURE UPLOADED

=> s 11

SAMPLE SEARCH INITIATED 14:07:37 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 28 TO ITERATE

100.0% PROCESSED 28 ITERATIONS 3 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 243 TO 877
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

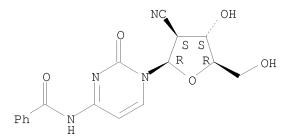
=> d 12 scan

L2 3 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN

IN Benzamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]-

MF C17 H16 N4 O5

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L2 3 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN

IN Cytidine, 2'-deoxy-2'-cyano- (9CI)

MF C10 H12 N4 O4

CI COM

Absolute stereochemistry.

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 3 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN

IN Carbamic acid,  $[16-[[1-(2-cyano-2-deoxy-\beta-D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]amino]-16-oxohexadecyl]-, phenylmethyl ester (9CI)$ 

MF C34 H49 N5 O7

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> file stnguide COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 0.98 1.20

FILE 'STNGUIDE' ENTERED AT 14:08:01 ON 26 JAN 2010 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 22, 2010 (20100122/UP).

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE Do you want to switch to the Registry File? Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 1.41

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 14:09:43 ON 26 JAN 2010 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2010 American Chemical Society (ACS)

Property values tagged with IC are from the  ${\tt ZIC/VINITI}$  data file provided by  ${\tt InfoChem.}$ 

STRUCTURE FILE UPDATES: 25 JAN 2010 HIGHEST RN 1203540-14-0 DICTIONARY FILE UPDATES: 25 JAN 2010 HIGHEST RN 1203540-14-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>

Uploading C:\Program Files\STNEXP\Queries\10581585nucleoside2.str

chain nodes :
6 7 14 15 16 17 18 19 20 21 24 25 26 27 28 29 30 31 32 33 34

ring nodes :
1 2 3 4 5 8 9 10 11 12 13
chain bonds :
1-17 1-28 2-18 2-27 4-8 4-31 5-6 5-30 6-7 9-15 11-14 12-33 13-32 14-16
14-24 17-29 18-25 19-20 19-21 21-34 25-26
ring bonds :
1-2 1-5 2-3 3-4 4-5 8-9 8-13 9-10 10-11 11-12 12-13
exact/norm bonds :
1-2 1-5 1-17 2-3 3-4 4-5 4-8 6-7 8-9 8-13 9-10 9-15 10-11 11-12 11-14
12-13 14-24 19-20
exact bonds :
1-28 2-18 2-27 4-31 5-6 5-30 12-33 13-32 14-16 17-29 18-25 19-21 21-34
25-26

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS

31:CLASS 32:CLASS

33:CLASS 34:CLASS

### L3 STRUCTURE UPLOADED

=> s 13

SAMPLE SEARCH INITIATED 14:09:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 28 TO ITERATE

100.0% PROCESSED 28 ITERATIONS 3 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 243 TO 877
PROJECTED ANSWERS: 3 TO 163

L4 3 SEA SSS SAM L3

=> d 14 scan

L4 3 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN

IN Carbamic acid,  $[16-[[1-(2-cyano-2-deoxy-\beta-D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]amino]-16-oxohexadecyl]-, phenylmethyl ester (9CI)$ 

MF C34 H49 N5 O7

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L4 3 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN

IN Benzamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]-

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 3 ANSWERS REGISTRY COPYRIGHT 2010 ACS on STN

IN Cytidine, 2'-deoxy-2'-cyano- (9CI)

MF C10 H12 N4 O4

CI COM

Absolute stereochemistry.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> 0

0 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> d 13

L3 HAS NO ANSWERS

L3 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s 13 sss full

FULL SEARCH INITIATED 14:10:45 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 848 TO ITERATE

100.0% PROCESSED 848 ITERATIONS

SEARCH TIME: 00.00.01

L5 67 SEA SSS FUL L3

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 192.03 193.44

67 ANSWERS

FULL ESTIMATED COST

FILE 'HCAPLUS' ENTERED AT 14:10:49 ON 26 JAN 2010 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 26 Jan 2010 VOL 152 ISS 5
FILE LAST UPDATED: 25 Jan 2010 (20100125/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2009

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 15/thu

80 L5

1207596 THU/RL

L6 61 L5/THU

(L5 (L) THU/RL)

=> s cancer or tumor or neopla?

440584 CANCER

529823 TUMOR

630275 NEOPLA?

L7 974388 CANCER OR TUMOR OR NEOPLA?

 $\Rightarrow$  s 16 and 17

L8 49 L6 AND L7

```
=> s 18 and (PY<2004 or AY<2004 or PRY<2004)
      24054885 PY<2004
       4830892 AY<2004
       4304454 PRY<2004
            22 L8 AND (PY<2004 OR AY<2004 OR PRY<2004)
1.9
=> d 19 1-22 ti abs bib hitstr
L9
     ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
     Combination of a CDK inhibitor and CS-682 or a metabolite thereof
ΤI
     A first aspect of the invention relates to a combination comprising a CDK
AB
     inhibitor and 1-(2-C-cyano-2-dioxy-\beta-D-arabino-pentofuranosyl)-N4-
     palmitoyl cytosine, or a metabolite thereof. A second aspect of the
     invention relates to a pharmaceutical product comprising a CDK inhibitor
     and 1-(2-C-cyano-2-dioxy-\beta-D-arabino-pentofuranosyl)-N4-palmitoyl
     cytosine, or a metabolite thereof, as a combined preparation for simultaneous,
     sequential or sep. use in therapy. A third aspect of the invention
     relates to a method of treating a proliferative disorder, said method
     comprising simultaneously, sequentially or sep. administering a CDK
     inhibitor and 1-(2-C-cyano-2-dioxy-\beta-D-arabino-pentofuranosyl)-N4-
     palmitoyl cytosine, or a metabolite thereof, to a subject.
ΑN
     2005:523291 HCAPLUS <<LOGINID::20100126>>
DN
     143:48129
ΤI
     Combination of a CDK inhibitor and CS-682 or a metabolite thereof
     Green, Simon; Sleigh, Roger Neil
ΙN
     Cyclacel Limited, UK
PΑ
     PCT Int. Appl., 27 pp.
SO
     CODEN: PIXXD2
DT
    Patent
    English
LA
FAN.CNT 1
    PATENT NO.
                       KIND DATE APPLICATION NO. DATE
                                          _____
                       ____
                               _____
    WO 2005053699
                        A1 20050616 WO 2004-GB5081
                                                                 20041203 <--
PΙ
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
            MR, NE, SN, TD, TG
     EP 1711185
                               20061018
                                          EP 2004-805910
                                                                  20041203 <--
                         Α1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
                               20070524 JP 2006-542014
     JP 2007513132
                        Т
                                                                  20041203 <--
     US 20070270442
                               20071122
                                          US 2007-581585
                                                                  20070420 <--
                         Α1
PRAI GB 2003-28180
                         Α
                               20031204
                                         <--
     WO 2004-GB5081 W
                               20041203
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
     151823-14-2, CS-682
     RL: PEP (Physical, engineering or chemical process); PYP (Physical
     process); THU (Therapeutic use); BIOL (Biological study); PROC
     (Process); USES (Uses)
        (antiproliferative combination of a CDK inhibitor and CS-682 or a
        metabolite thereof)
RN
     151823-14-2 HCAPLUS
     Hexadecanamide, N-[1-(2-cyano-2-deoxy-\beta-D-arabinofuranosy1)-1,2-
CN
```

## dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS) RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

N4-substituted CNDAC derivatives for pancreatic cancer treatment TΙ

N4-substituted derivs. of the known antitumor compound AΒ  $1-(2-C-cyano-2-deoxy-\beta-D-arabinopentofuranosyl)$ cytosine (CNDAC) are useful in treatment of pancreatic cancer, especially as an adjuvant treatment and especially over long-term administration. Compds. of the invention include e.g. the N4-palmitoyl derivative (CS-682).

ΑN 2005:14137 HCAPLUS <<LOGINID::20100126>>

142:86630 DN

ΤI N4-substituted CNDAC derivatives for pancreatic cancer treatment

ΙN Wang, Xiaoen; Wang, Jin Wei

Anticancer, Inc., USA PΑ

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.	CNT	1																	
		CENT				KIN		DATE					ION I				ATE		
PI	WO	2005 2005	0002	0 4		A2				,							0040	 521 ·	<
	WO		AE, CN, GE, LK,	AG, CO, GH, LR,	AL, CR, GM, LS,	AM, CU, HR, LT,	AT, CZ, HU, LU,	AU, DE, ID, LV, PL,	AZ, DK, IL, MA,	BA, DM, IN, MD,	DZ, IS, MG,	EC, JP, MK,	EE, KE, MN,	EG, KG, MW,	ES, KP, MX,	FI, KR, MZ,	GB, KZ, NA,	GD, LC, NI,	
		RW:	TJ, BW, AZ, EE, SI,	TM, GH, BY, ES, SK,	TN, GM, KG, FI, TR,	TR, KE, KZ, FR,	TT, LS, MD, GB,	TZ, MW, RU, GR, CF,	UA, MZ, TJ, HU,	UG, NA, TM, IE,	US, SD, AT, IT,	UZ, SL, BE, LU,	VC, SZ, BG, MC,	VN, TZ, CH, NL,	YU, UG, CY, PL,	ZA, ZM, CZ, PT,	ZM, ZW, DE, RO,	ZW AM, DK, SE,	
	AU CA CN CN EP	SN, TD, 20050014716 2004251598 2525589 1791415 100488516 1677805 R: BE, CH, 2006528989			DE,	A1 A C A2 FR,	GB,	2005 2005 2006 2009 2006 LI 2006	0106 0106 0621 0520 0712		AU 2 CA 2 CN 2 EP 2 JP 2	004- 004- 004- 004-	2515 2525 8001 7529	98 589 3774 20		2 2 2 2	0040 0040 0040 0040	521 · 521 · 521 ·	< < <
PRAI	US 2003-472529P P 2003052						0521	1 <											

WO 2004-US15997 20040521 W ΙT 135598-68-4D, derivs. 151823-14-2D, CS 682, derivs. 151823-42-6D, derivs. 151823-35-7D, derivs. 819805-91-9D, derivs. RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (N4-substituted CNDAC derivs. for pancreatic cancer treatment) RN 135598-68-4 HCAPLUS 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-CN (CA INDEX NAME)

Absolute stereochemistry.

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

RN 151823-35-7 HCAPLUS

CN Octadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

RN 151823-42-6 HCAPLUS

CN Tetradecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

RN 819805-91-9 HCAPLUS

CN 9-Octadecenamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]-, (9Z)- (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

Me (CH<sub>2</sub>) 
$$\frac{1}{7}$$
  $\frac{1}{2}$  (CH<sub>2</sub>)  $\frac{1}{7}$   $\frac{1}{1}$  NH

OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS) RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Synergistic treatment of cancer using immunomers in conjunction with chemotherapeutic agents

AB The invention discloses the therapeutic use of immunostimulatory oligonucleotides and/or immunomers in combination with chemotherapeutic agents to provide a synergistic therapeutic effect.

AN 2004:1036851 HCAPLUS <<LOGINID::20100126>>

DN 142:696

TI Synergistic treatment of cancer using immunomers in conjunction with chemotherapeutic agents

IN Kandimalla, Ekambar R.; Agrawal, Sudhir; Wang, Dagin

PA Hybridon, Inc., USA

SO PCT Int. Appl., 106 pp. CODEN: PIXXD2

DT Patent

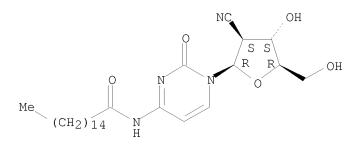
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004103301
                                20051103
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             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
    MARPAT 142:696
OS
ΙT
     151823-14-2, CS-682
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (immunostimulatory oligonucleotide and/or immunomer combination with
        chemotherapeutic agent for synergistic cancer treatment)
     151823-14-2 HCAPLUS
RN
     Hexadecanamide, N-[1-(2-cyano-2-deoxy-\beta-D-arabinofuranosyl)-1,2-
CN
```

Absolute stereochemistry.



OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

- TI Selective Antimetastatic Activity of Cytosine Analog CS-682 in a Red Fluorescent Protein Orthotopic Model of Pancreatic Cancer
- AB In this study we demonstrate the ability of a novel, p.o.-administered cytosine analog, CS-682, to effectively prolong survival and inhibit metastatic growth in an imageable orthotopic mouse model of pancreatic

cancer. MIA-PaCa-2-RFP pancreatic cancer cells were transduced with the Discosoma red fluorescent protein (RFP) and orthotopically implanted onto the pancreas of nude mice. Tumor RFP fluorescence facilitated real-time, sequential imaging, and quantification of primary and metastatic growth and dissemination in vivo. Mice were treated with various p.o. doses of CS-682 on a five times per wk schedule until death. At a dose of 40 mg/kg, CS-682 prolonged survival compared with untreated animals (median survival 35 days vs. 17 days; P = 0.0008). At nontoxic doses, CS-682 effectively suppressed the rate of primary tumor growth. CS-682 also decreased the development of malignant ascites and the formation of metastases, which were reduced significantly in number in the diaphragm, lymph nodes, liver, and kidney. Selective RFP tumor fluorescence enabled noninvasive real-time comparison between groups during treatment and facilitated identification of micrometastases in solid organs at autopsy. Thus, we have demonstrated that CS-682 is an efficacious antimetastatic agent that significantly prolongs survival in an orthotopic model of pancreatic cancer. The antimetastatic efficacy of CS-682 and its p.o. availability confer significant advantages and clin. potential to this agent for pancreatic cancer.

AN 2003:733802 HCAPLUS <<LOGINID::20100126>>

DN 140:87233

TI Selective Antimetastatic Activity of Cytosine Analog CS-682 in a Red Fluorescent Protein Orthotopic Model of Pancreatic Cancer

AU Katz, Matthew H.; Bouvet, Michael; Takimoto, Shinako; Spivack, Daniel; Moossa, Abdool R.; Hoffman, Robert M.

CS Department of Surgery, University of California at San Diego, San Diego, CA, 92161, USA

SO Cancer Research (2003), 63(17), 5521-5525 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

IT 151823-14-2, CS-682

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L9 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI High-Resolution Magnetic Resonance Imaging of the Efficacy of the Cytosine Analogue 1-[2-C-Cyano-2-deoxy- $\beta$ -D-arabino-pentofuranosyl]-N4-palmitoyl Cytosine (CS-682) in a Liver-Metastasis Athymic Nude Mouse Model
- High-resolution magnetic resonance (MR) imaging techniques in a liver AΒ metastatic mouse model were used to assess CS-682, a novel 2'-deoxycytidine analog of  $1-[2-C-cyano-2-deoxy-\beta-D-arabino$ pentofuranosyl]-N4-palmitoyl cytosine. The efficacy of CS-682 was visualized in real time by MR imaging of initial seeding and subsequent growth of liver metastases. The relative therapeutic efficacies of CS-682 and two agents used clin., gemcitabine [2'-deoxy-2',2'-difluorocytidine monohydrochloride (DFDC)] and 5-fluorouracil (5-FU), were compared in this model. CS-682 was found to exhibit superior efficacy by delaying the onset and inhibiting the growth of liver metastasis compared with gemcitabine, 5-FU, and control. The overall occurrence of metastases was decreased 62% by CS-682, 18% by DFDC, and 35% by 5-FU. CS-682 increased the life span of the treated animals significantly, by 28 days above the 29-day median survival without treatment, compared with 11 days by DFDC and  $1\overline{4}$  days by 5-FU. The increased survival in CS-682-treated animals correlated with the antimetastatic activity of this compound These preclin. findings support the potential clin. utility of CS-682 in the treatment of liver metastasis.
- AN 2003:373234 HCAPLUS <<LOGINID::20100126>>
- DN 139:332554
- TI High-Resolution Magnetic Resonance Imaging of the Efficacy of the Cytosine Analogue 1-[2-C-Cyano-2-deoxy- $\beta$ -D-arabino-pentofuranosyl]-N4-palmitoyl Cytosine (CS-682) in a Liver-Metastasis Athymic Nude Mouse Model
- AU Wu, Ming; Mazurchuk, Richard; Chaudhary, Neeta D.; Spernyak, Joseph; Veith, Jean; Pera, Paula; Greco, William; Hoffman, Robert M.; Kobayashi, Tomowo; Bernacki, Ralph J.
- CS Departments of Pharmacology and Therapeutics and Molecular and Cellular Biophysics, Roswell Park Cancer Institute, Buffalo, NY, 14263, USA
- SO Cancer Research (2003), 63(10), 2477-2482 CODEN: CNREA8; ISSN: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English
- IT 151823-14-2, CS-682

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(high-resolution magnetic resonance imaging of efficacy of cytosine analog 1-[2-C-cyano-2-deoxy- $\beta$ -D-arabino-pentofuranosyl]-N4-palmitoyl cytosine (CS-682) in a liver-metastasis athymic nude mouse model)

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Role of body surface area in dosing of investigational anticancer agents in adults, 1991-2001

AB The prescribed dose of anticancer agents is most commonly calculated using body surface area as the only independent variable, and it has been shown that this approach still results in large inter-patient variability in drug exposure. Here, we retrospectively assessed the pharmacokinetics of 33 investigational agents tested in phase I trials from 1991 through 2001, as a function of body surface area in 1650 adult cancer, patients. Twelve of the drugs were administered orally, 19 were administered i.v., and two were administered by both routes. Body surface

area-based dosing was statistically significantly associated with a reduction in

inter-patient variability in drug clearance for only five of the 33 agents: docosahexaenoic acid (DHA)-paclitaxel, 5-fluorouracil/eniluracil, paclitaxel, temozolomide, and troxacitabine. These results do not support the use of body surface area in dose calcns. and suggest that alternate dosing strategies should be evaluated. We conclude that body surface area should not be used to determine starting doses of investigational agents in future phase I studies.

AN 2003:55812 HCAPLUS <<LOGINID::20100126>>

DN 139:223633

TI Role of body surface area in dosing of investigational anticancer agents in adults, 1991-2001

AU Baker, Sharyn D.; Verweij, Jaap; Rowinsky, Eric K.; Donehower, Ross C.; Schellens, Jan H. M.; Grochow, Louise B.; Sparreboom, Alex

CS Division of Experimental Therapeutics, The Sydney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA

SO Journal of the National Cancer Institute (2002), 94(24), 1883-1888

CODEN: JNCIEQ; ISSN: 0027-8874

PB Oxford University Press

DT Journal

LA English

IT 151823-14-2, CS-682

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(role of body surface area in dosing of investigational anticancer agents in adults)

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

- OSC.G 62 THERE ARE 62 CAPLUS RECORDS THAT CITE THIS RECORD (62 CITINGS) RE.CNT 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN L9
- TΙ Preparation of crystal of pyrimidine nucleoside derivative
- AB Crystals of a pyrimidine nucleoside derivative, namely 2'-cyano-2'-deoxy-N4-palmitoyl-1- $\beta$ -D-arabinofuranosylcytosine (I) having excellent antitumor activity in warm blooded animals, in particular human, are prepared by crystallization from anhydrous or water-containing Me acetate and

characterized by powder X-ray diffraction anal. They are improved in storage stability and easiness of handling and excellent in oral absorbability. Pharmaceutical compns. containing I, e.g. solution and aerosol, were prepared

- 2002:637691 HCAPLUS <<LOGINID::20100126>> ΑN
- 137:169744 DN
- Preparation of crystal of pyrimidine nucleoside derivative ΤI
- Takita, Takashi; Ohtsuka, Keiichi; Numagami, Eiji; Harashima, Susumu ΙN
- Sankyo Company, Limited, Japan PA
- SO PCT Int. Appl., 24 pp. CODEN: PIXXD2
- DTPatent

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		823-			~~1~.															

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic

use); BIOL (Biological study); PROC (Process); USES (Uses) (preparation of crystals of pyrimidine nucleoside derivative having excellent

antitumor activity)

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

# RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L9 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Methods for enhancing antibody-induced cell lysis and treating cancer
- AB The invention relates to methods and products for treating cancer
  . In particular the invention relates to combinations of nucleic acids
  and antibodies for the treatment and prevention of cancer. The
  invention also relates to diagnostic methods for screening cancer
  cells.
- AN 2001:935435 HCAPLUS <<LOGINID::20100126>>
- DN 136:84677
- TI Methods for enhancing antibody-induced cell lysis and treating cancer
- IN Weiner, George; Hartmann, Gunther
- PA University of Iowa Research Foundation, USA
- SO PCT Int. Appl., 312 pp.

CODEN: PIXXD2

- DT Patent
- LA English

FAN.CNT 1

FAN.	AN.CNT 1 PATENT NO.					KIND DATE					APPL	ICAT		DATE					
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	WO	2001-US20154	W	20010622	<	
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ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT IT 151823-14-2, CS-682

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (immunostimulatory nucleic acids and antibody specific to CD20, CD22, CD19 or CD40 for inducing cell lysis and treating cancer)

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Deletion mutants of human deoxycytidine kinase mRNA in cells resistant to antitumor cytosine nucleosides

We studied mutational events in deoxycytidine (dCyd) kinase mRNA AΒ expression, focusing on aberrant dCyd kinase mRNA, which has been frequently observed in established cell lines resistant to antitumor dCyd nucleoside analogs such as  $1-\beta-D$ -arabinofuranosyl cytosine (Ara-C), gemcitabine (dFdC) and 2'-C-cyano-2'-deoxy-1- $\beta$ -Darabinofuranosylcytosine (CNDAC). We describe here the expression of aberrant dCyd kinase mRNAs identified as splicing mutants. These mutants included deletions of the fifth exon in CNDAC-resistant cells (originating from HT-1080 cells), of the third exon in Ara-C-resistant cells (originating from SK-MEL-28 cells) and of the fourth exon in 2'-deoxy-2'-methylidenecytidine (DMDC)-resistant cells (originating from SK-MEL-28 cells). Various nucleoside-resistant cells originating from the same parental HT-1080 cells were established. The resulting cells expressed the same mRNA with deletion of the fifth exon, and the location of splicing was independent of the type of nucleosides used for the establishment of resistant cells. The deletion of the fifth exon in dCyd

kinase seems to be a target for acquisition of resistance to antitumor cytosine nucleosides. However, distinct mutations in the dCyd kinase gene seem to be associated with acquisition of resistance to different antitumor cytosine nucleosides.

- AN 2001:671059 HCAPLUS <<LOGINID::20100126>>
- DN 136:31393
- TI Deletion mutants of human deoxycytidine kinase mRNA in cells resistant to antitumor cytosine nucleosides
- AU Obata, Tohru; Endo, Yoshio; Tanaka, Motohiro; Uchida, Hiroyuki; Matsuda, Akira; Sasaki, Takuma
- CS Department of Experimental Therapeutics, Cancer Research Institute, Kanazawa University, Kanazawa, 920-0934, Japan
- SO Japanese Journal of Cancer Research (2001), 92(7), 793-798 CODEN: JJCREP; ISSN: 0910-5050
- PB Japanese Cancer Association
- DT Journal
- LA English
- IT 135598-68-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(deletion mutants of human deoxycytidine kinase mRNA in cells resistant to antitumor cytosine nucleosides)

- RN 135598-68-4 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

- OSC.G 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
- RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L9 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Targeting and anti-tumor efficacy of liposomal 5'-O-dipalmitoylphosphatidyl 2'-C-cyano-2'-deoxy-1- $\beta$ -d-arabino-pentofuranosylcytosine in mice lung bearing B16BL6 melanoma
- AB 2'-C-cyano-2'-deoxy-1- $\beta$ -d-arabinopentofuranosylcytosine (CNDAC) is a potent anticancer agent, and we previously observed that liposomal formulation of 5'-O-dipalmitoylphosphatidyl derivative of CNDAC (DPP-CNDAC) is desirable for targeting. For targeting to pulmonary cancer, we investigated the in vivo behavior of liposomes containing DPP-CNDAC by a non-invasive method using positron emission tomog. Liposomes composed of DPP-CNDAC and cholesterol (DPP-CNDAC/CH liposomes) were markedly accumulated in mice lung bearing B16BL6 melanoma. In metastatic pulmonary cancer model, DPP-CNDAC/CH liposomes significantly reduced the lung colonization in a dose-dependent manner. The activity was significantly superior to conventional liposomal formulation or soluble CNDAC. These results suggest that DPP-CNDAC/CH liposomes are useful for metastatic pulmonary cancer.
- AN 2000:895848 HCAPLUS <<LOGINID::20100126>>

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DN 134:290061
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- TI Targeting and anti-tumor efficacy of liposomal 5'-O-dipalmitoylphosphatidyl 2'-C-cyano-2'-deoxy-1- $\beta$ -d-arabino-pentofuranosylcytosine in mice lung bearing B16BL6 melanoma
- AU Asai, T.; Shuto, S.; Matsuda, A.; Kakiuchi, T.; Ohba, H.; Tsukada, H.; Oku, N.
- CS Department of Radiobiochemistry, School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, 422-8526, Japan
- SO Cancer Letters (Shannon, Ireland) (2001), 162(1), 49-56 CODEN: CALEDQ; ISSN: 0304-3835
- PB Elsevier Science Ireland Ltd.
- DT Journal
- LA English
- IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (targeting and antitumor efficacy of liposomal

- 5'-O-dipalmitoylphosphatidyl  $2'-C-cyano-2'-deoxy-1-\beta-d-arabino-pentofuranosylcytosine in mice lung bearing B16BL6 melanoma)$
- RN 135598-68-4 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

- OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
  RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
  ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L9 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Liposome preparation of fat-soluble antitumor drug
- AB The invention relates to a liposome preparation containing 1-(2'-cyano-2'-deoxy- $\beta$ -D-arabinopentofuranosyl)-N4-palmitoylcytosine acting as an antitumor agent, which exhibits high drug transfer to tumor tissue and high residence in such tissue and can be put to practical use.
- AN 2000:814316 HCAPLUS <<LOGINID::20100126>>
- DN 133:366425
- TI Liposome preparation of fat-soluble antitumor drug
- IN Kasuya, Yuji; Okada, Junichi; Hanaoka, Kenji; Kurakata, Shinichi; Matsuda, Akira; Sasaki, Takuma
- PA Sankyo Co., Ltd., Japan
- SO PCT Int. Appl., 53 pp. CODEN: PIXXD2
- DT Patent
- LA Japanese
- FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2000067760 A1 20001116 WO 2000-JP2993 20000510 <--PΤ W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, TR, US, ZA RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE JP 2001026544 20010130 JP 2000-136600 20000510 <--Α PRAI JP 1999-129639 Α 19990511 <--151823-14-2 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (liposome preparation of fat-soluble antitumor drug) 151823-14-2 HCAPLUS RNHexadecanamide,  $N-[1-(2-cyano-2-deoxy-\beta-D-arabinofuranosy1)-1,2-$ 

Absolute stereochemistry.

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

 ${\tt TI}$  Studies on the expression of deoxycytidine kinase gene in the CNDAC-resistant cell line

AB Ara-C and CNDAC are two effective antitumor chemotherapeutic agents which need phosphorylation by deoxycytidine kinase (dCK) for the activation of their cytotoxicity. In order to identify the reason for the drug resistance, the expression of dck mRNA in human tumor fibrosarcoma HT-1080 and its drug resistant cell line CN-20 was analyzed. The 799 bp coding region for the dck gene was amplified by the RT-PCR method from the total RNA of the parental cells, but the products from the resistant cells were two fragments: 799 bp and 683 bp. Compared with the normal fragment, there was a 116 bp deletion in the aberrant 683 bp fragment, which located in the fifth exon of the dck gene. Two point mutations had also been found in the 799 bp fragment. These results suggest that the acquired resistance to CNDAC can be attributed to a deficiency of dCK activity, which might be based on the genetic mutation of the dck gene.

AN 2000:653106 HCAPLUS <<LOGINID::20100126>>

DN 133:344311

 ${
m TI}$  Studies on the expression of deoxycytidine kinase gene in the  ${
m CNDAC\text{-}resistant}$  cell line

AU Han, Ning; Ming, Zheng-huan

CS College of Life Sciences, Zhejiang University, Hangzhou, 310012, Peop. Rep. China

SO Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao (2000), 16(4), 520-523

CODEN: ZSHXF2; ISSN: 1007-7626

PB Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao Bianweihui

DT Journal

LA Chinese

IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CNDAC; studies on the expression of deoxycytidine kinase gene in the CNDAC-resistant cell line)

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

- L9 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Liposome compositions containing antitumor drugs
- AB Disclosed are liposome compns. containing  $1-(2\text{'-cyano-2'-deoxy-}\beta-D-\text{arabino-pentofranosyl})\,\text{cytosine (CNDAC)}$  antitutor agent, sterols, and phosphatidylcholines, which are excellent in the accumulation in tumor tissues and the retention therein and thus exert a favorable antitumor activity. Multilayer liposomes were prepared from CNDAC·HCl, dipalmitoylphosphatidylcholine, dipalmitoylphosphatidylglycerol, cholesterol, N-monomethoxypolyethylene glycolsuccinyl-distearoylphosphatidylethanolamine, glucose, trehalose, and water, and the antitumor activity was examined
- AN 2000:592565 HCAPLUS <<LOGINID::20100126>>
- DN 133:168414
- TI Liposome compositions containing antitumor drugs
- IN Kasuya, Yuji; Okada, Junichi; Hanaoka, Kenji; Kurakata, Shinichi; Matsuda, Akira; Sasaki, Takuma
- PA Sankyo Company, Ltd., Japan
- SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

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			US,	ZA															
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			PT,	SE															
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IT 134665-72-8 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antitumor liposome compns. containing CNDAC and sterols and

phosphatidylcholines and phosphatidylethanolamine derivs.) 134665-72-8 HCAPLUS 2(1H)-Pyrimidinone,  $4-amino-1-(2-cyano-2-deoxy-\beta-D-arabinofuranosyl)-$ 

, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

RN

CN

● HCl

RN 135598-68-4 HCAPLUS CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Antitumor activity and novel DNA-self-strand-breaking mechanism of CNDAC  $(1-(2-C-cyano-2-deoxy-\beta-D-arabino-pentofuranosyl)$ cytosine) and its N4-palmitoyl derivative (CS-682)

We have studied the antitumor activity and the novel DNA-self-strand-breaking mechanism of CNDAC (1-(2-C-cyano-2-deoxy- $\beta$ -D-arabino-pentofuranosyl)cytosine) and its N4-palmitoyl derivative (CS-682). In vitro, CS-682 showed strong cytotoxicity against human tumor cells comparable with that of CNDAC; both compds. displayed a similar broad spectrum. In vivo, however, orally administered CS-682 showed a more potent activity against human tumor xenografts than CNDAC, 5'-deoxy-5-fluorouridine, 5-fluorouracil and 2',2'-difluorodeoxycytidine. Moreover, CS-682 was effective against various human organ tumor xenografts at a wide dose range and with low toxicity, and was effective against P388 leukemic cells resistant to mitomycin-C, vincristine, 5-fluorouracil or cisplatin in syngeneic mice. CNDAC, an active metabolite of CS-682, had a prolonged

plasma half-life after repeated oral administrations of CS-682 but not after oral administrations of CNDAC itself. This difference may partially explain the higher antitumor activity of CS-682 relative to CNDAC. In both CNDAC- and CS-682-treated carcinoma cells, CNDAC 5'-triphosphate (CNDACTP) was generated and incorporated into a DNA strand. High performance liquid chromatog. (HPLC) and mass spectrometric anal. of the nucleosides prepared by digestion of the DNA from the CNDAC-treated cells detected ddCNC (2'-C-cyano-2',3'-didehydro-2',3'-dideoxycytidine), which was shown to be generated only when the self-strand-breakage of CNDACTP-incorporated DNA occurred. The cytotoxicity of CNDAC was completely abrogated by the addition of 2'-deoxycytidine and was low against cells with decreased deoxycytidine kinase. Our results suggest that CNDAC is converted to CNDACMP by deoxycytidine kinase and that the resulting CNDACTP incorporated into a DNA strand as CNDACMP may induce DNA-self-strand-breakage. This novel DNA-self-strand-breaking mechanism may contribute to the potent antitumor activity of CS-682.

AN 1999:438485 HCAPLUS <<LOGINID::20100126>>

DN 131:266648

TI Antitumor activity and novel DNA-self-strand-breaking mechanism of CNDAC  $(1-(2-C-cyano-2-deoxy-\beta-D-arabino-pentofuranosyl)$  cytosine) and its N4-palmitoyl derivative (CS-682)

AU Hanaoka, Kenji; Suzuki, Masako; Kobayashi, Tomowo; Tanzawa, Fumie; Tanaka, Kazuo; Shibayama, Takahiro; Miura, Shinichi; Ikeda, Tomoko; Iwabuchi, Haruo; Nakagawa, Akihiko; Mitsuhashi, Yoshihiro; Hisaoka, Masashi; Kaneko, Masakatsu; Tomida, Akihiro; Wataya, Yusuke; Nomura, Tatsuji; Sasaki, Takuma; Matsuda, Akira; Tsuruo, Takashi; Kurakata, Shinichi

CS Biological Research Laboratories, Sankyo Co., Ltd., Tokyo, 140-8710, Japan

SO International Journal of Cancer (1999), 82(2), 226-236 CODEN: IJCNAW; ISSN: 0020-7136

PB Wiley-Liss, Inc.

DT Journal

LA English

IT 135598-68-4 151823-14-2, CS-682

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(antitumor activity and DNA-self-strand-breaking mechanism of 2'-deoxycytidine analog CNDAC and its N4-palmitoyl derivative CS-682)

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Therapy of lung metastatic cancer by lung-targeted liposomal 5'-O-dipalmitoylphosphatidyl 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabino-pentofuranosyl-cytosine

AΒ  $2'-C-cyano-2'-deoxy-1-\beta-D-arabino-pentofuranosylcytosine (CNDAC), a$ novel antitumor nucleoside antimetabolite, has a new mechanism of action for damaging tumor cells. This compound showed potent growth inhibitory activity against various kinds of human tumor cells both in vitro and in vivo. Furthermore, 5'-phosphatidylation of the compound enhanced the antitumor activity. We liposomalized 5'-O-dipalmitoylphosphatidyl derivative of CNDAC(DPP-CNDAC) and investigated the effect of DPP-CNDAC incorporation on the in vivo behavior of these liposomes by a non-invasive method using positron emission tomog. (PET). Interestingly, liposomes composed of DPP-CNDAC and cholesterol(DPP-CNDAC/CH liposomes) were observed to have a tendency to accumulate in lungs. Furthermore, this accumulation was markedly enhanced in the mice bearing lung metastatic cancer. Therefore, we attempted to use these CNDAC/CH liposomes for lung targeting and to examine the therapeutic efficacy against lung metastatic cancer. In exptl. model using highly lung metastatic murine B16BL6 melanoma cells, these liposomes significantly reduced the number of lung tumor colonies as well as the size of them in a dose dependent manner. On the contrary, reduced lung colonization was not seen by use of the formulation of conventional liposomes or soluble CNDAC. These results were coincident with the data of PET anal., and suggesting the usefulness of DPP-CNDAC/CH liposomes for curing lung metastasis.

AN 1999:383158 HCAPLUS <<LOGINID::20100126>>

DN 131:233467

- TI Therapy of lung metastatic cancer by lung-targeted liposomal 5'-O-dipalmitoylphosphatidyl 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabino-pentofuranosyl-cytosine
- AU Asai, Tomohiro; Kurohane, Kohta; Okada, Shoji; Shuto, Satoshi; Awano, Hirokazu; Matsuda, Akira; Tsukada, Hideo; Oku, Naoto
- CS School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, 422-8526, Japan
- SO Drug Delivery System (1999), 14(2), 103-108 CODEN: DDSYEI; ISSN: 0913-5006
- PB Nippon DDS Gakkai Jimukyoku
- DT Journal
- LA Japanese
- IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (therapy of lung metastatic cancer by targeted liposomal

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5'-O-dipalmitoylphosphatidyl 2'-C-cyano-2'-deoxy-1-\beta-D-arabino-pentofuranosyl-cytosine)\\ RN 135598-68-4 HCAPLUS\\ CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy-\beta-D-arabinofuranosyl)-(CA INDEX NAME)
```

Absolute stereochemistry.

### OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L9 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Determinants in chemosensitivity of oncogene-transformed NIH3T3 cells to  $2'-C-cyano-2'-deoxy-1-\beta-D-arabinofuranosylcytosine$ 

AB 2'-C-Cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine (CNDAC) is a novel 2'-deoxycytidine (dCyd) analog with potent antitumor activity. To elucidate the determinants of chemosensitivity to CNDAC, the intracellular accumulation of CNDAC and the activities of dCyd kinase and cytidine deaminase were investigated in transformed NIH 3T3 cells with different genetic bases. The results indicate that the primary determinants of chemosensitivity to CNDAC are different in each cell type, but membrane transportation and the enzyme activities of dCyd kinase and cytidine deaminase are critical factors underlying the antitumor action of CNDAC. Moreover, the expression or function of these factors appears to be influenced by the activation of various oncogenes.

AN 1999:169183 HCAPLUS <<LOGINID::20100126>>

DN 131:27524

TI Determinants in chemosensitivity of oncogene-transformed NIH3T3 cells to 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine

AU Zhang, Min; Endo, Yoshio; Sasaki, Takuma

CS Department of Experimental Therapeutics, Cancer Research Institute, Kanazawa University, Kanazawa, 920-0934, Japan

SO International Journal of Oncology (1999), 14(3), 543-549 CODEN: IJONES; ISSN: 1019-6439

PB International Journal of Oncology

DT Journal

LA English

IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(determinants in chemosensitivity of oncogene-transformed NIH3T3 cells to 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine)

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L9 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Why is the DNA-strand-breaker, PCNDAC, effective to solid tumors?
- AB A review with 12 refs., on action mechanism of antitumor 2'-deoxycytidine derivative, PCNDAC, a prodrug of CNDAC, discussing intracellular transport of antitumor nucleoside, feedback inhibitory action of triphosphates on mouse deoxycytidine kinase, inhibition of DNA formation by DNA-strand breaking, and apoptosis induction in human solid tumors.
- AN 1998:621620 HCAPLUS <<LOGINID::20100126>>
- DN 130:96
- TI Why is the DNA-strand-breaker, PCNDAC, effective to solid tumors?
- AU Matsuda, Akira; Sasaki, Takuma
- CS Grad. Sch. Pharm. Sci., Hokkaido Univ., Sapporo, 060-0812, Japan
- SO Tanpakushitsu Kakusan Koso (1998), 43(13), 1981-1989 CODEN: TAKKAJ; ISSN: 0039-9450
- PB Kyoritsu Shuppan
- DT Journal; General Review
- LA Japanese
- IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)

(action mechanism of DNA-strand-breaker PCNDAC on solid tumors)

- RN 135598-68-4 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

IT 151823-14-2

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(action mechanism of DNA-strand-breaker PCNDAC on solid tumors)

RN 151823-14-2 HCAPLUS

CN Hexadecanamide, N-[1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-1,2-dihydro-2-oxo-4-pyrimidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Development and biochemical characterization of a  $2'-C-cyano-2'-deoxy-1-\beta-d-arabino-pentofuranosylcytosine$  (CNDAC)-resistant variant of the human fibrosarcoma cell line HT-1080 AB  $2'-C-Cyano-2'-deoxy-1-\beta-d-arabino-pentofuranosylcytosine$  (CNDAC) is

 $2'-C-Cyano-2'-deoxy-1-\beta-d-arabino-pentofuranosylcytosine (CNDAC)$  is an antitumor nucleoside with a novel chemical structure that exerts potent antitumor activity against various human tumor cells in vitro and in vivo. To be active it needs to be phosphorylated by deoxycytidine (dCyd) kinase. The authors induced resistance to CNDAC in the human fibrosarcoma cell line HT-1080 by exposure to increasing concns. of CNDAC. The resistant cells showed over 560 times higher resistance as compared to that of the parental HT-1080 cells and were cross-resistant to the other 2'-deoxycytidine derivs. The dCyd kinase mRNA expression of the resistant cells decreased and there was the expression of aberrant mRNA of dCyd kinase which contained a 116-nucleotide deletion within the coding region, corresponding to the fifth exon of the gene. The dCyd kinase enzymic activity of the resistant cells was deficient. The initial uptake of CNDAC into the resistant cells was similar to that of the parental cells. However, the incorporation of CNDAC into the DNA fraction of the resistant cells was significantly less than that of the parent cells. These results led the authors to conclude that the acquired resistance to CNDAC can be attributed to a deficiency of dCyd kinase activity, which should be based on a remarkable decrease in mRNA expression and genetic mutation of the dCyd kinase gene, but not on cellular CNDAC accumulation.

AN 1998:15291 HCAPLUS <<LOGINID::20100126>>

DN 128:175860

OREF 128:34515a,34518a

TI Development and biochemical characterization of a  $2'-C-cyano-2'-deoxy-1-\beta-d-arabino-pentofuranosylcytosine$  (CNDAC)-resistant variant of the human fibrosarcoma cell line HT-1080 AU Obata, Tohru; Endo, Yoshio; Tanaka, Motohiro; Matsuda, Akira; Sasaki,

Takuma

CS Cancer Research Institute, Department of Experimental Therapeutics and Development Center for Molecular Target Drugs, Kanazawa University, 13-1 Takaramachi, Kanazawa, 920, Japan

SO Cancer Letters (Shannon, Ireland) (1998), 123(1), 53-61 CODEN: CALEDQ; ISSN: 0304-3835

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic

use); BIOL (Biological study); PROC (Process); USES (Uses) (development of cyanodeoxydarabinopentofuranosylcytosine-resistant human fibrosarcoma cell line HT-1080 in relation to deoxycytidine kinase expression and incorporation into DNA)

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI Design of a new antitumor nucleoside, CNDAC, against solid tumors

AΒ A review with 9 refs. The design, antitumor activity in vitro as well as in vivo, and mechanism of CNDAC have been described. CNDAC  $(2'-C-Cyano-2'-deoxy-1-\beta-D-arabinofuranosylcytosine)$  had potent antitumor effects against various solid tumors in vitro as well as in vivo. CNDAC was phosphorylated by deoxycytidine kinase, followed by certain nucleotide kinases to afford its 5'-triphosphate (CNDACTP), which was a potent inhibitor of DNA polymerase  $\alpha$ . Using a chain-extension method with Vent (exo-) DNA polymerase and a short primer/template system, the authors found that CNDACTP was incorporated into the primer. After further chain-extension reaction of the primer containing CNDAC at the 3'-terminus, chain elongation was not observed Therefore, CNDACTP appeared to act as a chain-terminator. Analyses of the structure of the 3'-terminus in the primer revealed the presence of ddCNC together with CNDAC and CNDC. The existence of ddCNC in the 3'-end of the primer would be due to the self-strand-break by the nucleotide incorporated next to CNDAC.

AN 1996:143402 HCAPLUS <<LOGINID::20100126>>

DN 124:249363

OREF 124:45845a,45848a

TI Design of a new antitumor nucleoside, CNDAC, against solid tumors

AU Matsuda, Akira

CS Fac. Pharm. Sci., Hokkaido Univ., Japan

SO Gan to Kagaku Ryoho (1996), 23(2), 202-10 CODEN: GTKRDX; ISSN: 0385-0684

PB Gan to Kagaku Ryohosha

DT Journal; General Review

LA Japanese

IT 135598-68-4

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CNDAC; design of a new antitumor nucleoside, CNDAC, against solid tumors)

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-

Absolute stereochemistry.

## OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L9 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN

TI  $2'-C-Cyano-2'-deoxy-1-\beta-D-arabinofuranosylcytosine$  (CNDAC): a mechanism-based DNA-strand-breaking antitumor nucleoside

AB The antitumor mechanism of action of

 $2\text{'-C-cyano-}2\text{'-deoxy-}1\text{-}\beta\text{-}D\text{-}arabinofuranosylcytosine}$  (CNDAC) has been examined CNDAC was designed as a potentially DNA-self-strand-breaking nucleoside. It has potent antitumor effects against various solid tumors in vitro as well as in vivo. Using a chain-extension method with Vent (exo-) DNA polymerase and a short primer/template system, the authors found that 5'-triphosphate of CNDAC (CNDACTP) was incorporated into the primer at a site opposite a guanine residue in the template. After further chain-extension reaction of the primer containing CNDAC at the 3'-terminus, chain elongation was not observed. Therefore, CNDACTP appeared to act as a chain-terminator. Analyses of the structure of the 3'-terminus in the primer revealed

 $2'\text{-C-cyano-}2',3'\text{-didehydro-}2',3'\text{-dideoxycytidine} \ (ddCNC) \ together with CNDAC and <math display="inline">2'\text{-C-cyano-}2'\text{-deoxy-}1\text{-}\beta\text{-D-ribofuranosylcytosine} \ (CNDC)$  . The existence of ddCNC in the 3'-end of the primer would be due to the self-strand-break by the nucleotide incorporated next to CNDAC. The authors also found that CNDAC was epimerized to CNDC in near-neutral to alkaline media. Therefore, CNDC found in the primer was epimerized after incorporation of CNDACTP into the primer. The authors also described the metabolism of CNDAC.

AN 1995:631018 HCAPLUS <<LOGINID::20100126>>

DN 123:132187

OREF 123:23181a,23184a

TI 2'-C-Cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine (CNDAC): a mechanism-based DNA-strand-breaking antitumor nucleoside

AU Matsuda, Akira; Azuma, Atsushi

CS Faculty Pharmaceutical Sciences, Hokkaido University, Sapporo, 060, Japan

SO Nucleosides & Nucleotides (1995), 14(3-5), 461-71 CODEN: NUNUD5; ISSN: 0732-8311

PB Dekker

DT Journal

LA English

IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(cyanodeoxyarabinofuranosylcytosine as mechanism-based DNA-strand-breaking antitumor nucleoside)

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-

(CA INDEX NAME)

Absolute stereochemistry.

IT 140859-14-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)

(cyanodeoxyarabinofuranosylcytosine as mechanism-based DNA-strand-breaking antitumor nucleoside)

RN 140859-14-9 HCAPLUS

CN Cytidine, 2'-deoxy-2'-cyano- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

### OSC.G 39 THERE ARE 39 CAPLUS RECORDS THAT CITE THIS RECORD (39 CITINGS)

- L9 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Antitumor activity of a novel nucleoside, 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine (CNDAC) against murine and human tumors
- The antitumor effects of 2'-C-cyano-2'-deoxy-1- $\beta$ -D-AB arabinofuranosylcytosine (CNDAC), a synthetic ara-C derivative, were examined and compared with that of ara-C in murine tumors and in various human tumors using three different chemosensitivity tests. CNDAC extended the life span of mice bearing P388 leukemia. CNDAC had a unique in vitro antitumor spectrum for human cancers different from that of ara-C. Compared with ara-C, CNDAC was more effective in 10 human tumors (2 lung, 4 stomach and 4 osteosarcoma), equal in 2 tumors (lung and fibrosarcoma) and less potent in 11 tumors (4 lung, 4 osteosarcoma, bladder, renal and epidermoid). Characteristically CNDAC showed excellent activities against tumors, refractory to ara-C, such as HT-1080 human fibrosarcoma implanted in chick embryos or athymic mice, although its cytotoxicity against HT-1080 was almost equal to that of ara-C. Thus, CNDAC is an interesting and promising agent that should be considered for further detailed preclin. evaluation.
- AN 1992:462502 HCAPLUS <<LOGINID::20100126>>
- DN 117:62502

OREF 117:10787a,10790a

- TI Antitumor activity of a novel nucleoside, 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine (CNDAC) against murine and human tumors
- AU Tanaka, Motohiro; Matsuda, Akira; Terao, Tomoko; Sasaki, Takuma
- CS Cancer Res. Inst., Kanazawa Univ., Kanazawa, 920, Japan
- SO Cancer Letters (Shannon, Ireland) (1992), 64(1), 67-74 CODEN: CALEDQ; ISSN: 0304-3835
- DT Journal
- LA English
- IT 135598-68-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neoplasm inhibition by, in human and laboratory animal cells)

- RN 135598-68-4 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

OSC.G 50 THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (50 CITINGS)

- L9 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Nucleosides and nucleotides. 100. 2'-C-Cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine (CNDAC): design of a potential mechanism-based DNA-strand-breaking antineoplastic nucleoside

GΙ

AB A new type of antineoplastic nucleoside,

 $2'\text{-C-cyano-}2'\text{-deoxy-}\beta\text{-D-arabinofuranosylcytosine}$  (CNDAC) (I) has been designed based on the hypothesis that if a nucleoside had a chemical reactivity to cleave a DNA strand after its incorporation into the DNA mol. it could exert a unique antineoplastic activity. I was synthesized from the corresponding 2'-keto nucleoside via cyanohydrin formation followed by radical deoxygenation of the phenoxyghiocarbonate of the 2'-hydroxy group. I has not only potent antileukemic activity against mouse L1210 cells (IC50 = 0.21  $\mu\text{g/mL}$ ) but also potent inhibitory activity of growth of various human tumor cells in vitro with IC50 values 0.04 to 6.8  $\mu\text{g/mL}$ . In vivo antitumor activity of I against p388 was also examined When I was i.p. administered once a day for 10 days continuously with a dose of 20 mg/kg, 5 out of 6 mice survived over 60 days (T/C >600%). Thus I is a promising antitumor agent that should be considered for further detailed preclin. evaluation.

AN 1991:526535 HCAPLUS <<LOGINID::20100126>>

DN 115:126535

OREF 115:21449a,21452a

TI Nucleosides and nucleotides. 100. 2'-C-Cyano-2'-deoxy-1- $\beta$ -D-arabinofuranosylcytosine (CNDAC): design of a potential mechanism-based DNA-strand-breaking antineoplastic nucleoside

AU Matsuda, Akira; Nakajima, Yuki; Azuma, Atsushi; Tanaka, Motohiro; Sasaki, Takuma

CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan

SO Journal of Medicinal Chemistry (1991), 34(9), 2917-19 CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

OS CASREACT 115:126535

RN 134665-72-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 135598-68-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-cyano-2-deoxy- $\beta$ -D-arabinofuranosyl)- (CA INDEX NAME)

Absolute stereochemistry.

## OSC.G 57 THERE ARE 57 CAPLUS RECORDS THAT CITE THIS RECORD (57 CITINGS)

=> file registry		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	133.64	327.08
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-18.70	-18.70

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STRUCTURE FILE UPDATES: 25 JAN 2010 HIGHEST RN 1203540-14-0 DICTIONARY FILE UPDATES: 25 JAN 2010 HIGHEST RN 1203540-14-0

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

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http://www.cas.org/support/stngen/stndoc/properties.html

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E3	T>	ROSCOVITINE/CN
E 4	1	ROSCOVITINE CARBOXYLIC ACID/CN
E5	1	ROSE ACETONE/CN
E6	1	ROSE ALLOY/CN
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E8	1	ROSE BD/CN
E9	1	ROSE BENGAL/CN
E10	1	ROSE BENGAL (1311) SODIUM/CN

E11 1 ROSE BENGAL 3-IODOPROPYL ESTER MONOSODIUM SALT/CN E12 1 ROSE BENGAL 4-BROMOBUTYL ESTER MONOSODIUM SALT/CN

=> s E2-E3

1 ROSCOVITIN/CN 1 ROSCOVITINE/CN

L10 1 (ROSCOVITIN/CN OR ROSCOVITINE/CN)

=> file hcaplus

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
11.49
338.57

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION

CA SUBSCRIBER PRICE

0.00
-18.70

FILE 'HCAPLUS' ENTERED AT 14:12:12 ON 26 JAN 2010 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 26 Jan 2010 VOL 152 ISS 5
FILE LAST UPDATED: 25 Jan 2010 (20100125/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2009

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 110 L11 600 L10

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FILE 'REGISTRY' ENTERED AT 14:01:17 ON 26 JAN 2010

EXP 1/(2-CYANO-2-DEOXY-/CN

EXP 1-(2-CYANO-2-DEOXY-/CN

EXP 1-(2-C-CYANO-2-DEOXY-/CN

L1 STRUCTURE UPLOADED

L2 3 S L1

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     FILE 'REGISTRY' ENTERED AT 14:09:43 ON 26 JAN 2010
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L4
               3 S L3
L5
              67 S L3 SSS FULL
     FILE 'HCAPLUS' ENTERED AT 14:10:49 ON 26 JAN 2010
              61 S L5/THU
L6
L7
          974388 S CANCER OR TUMOR OR NEOPLA?
L8
              49 S L6 AND L7
L9
              22 S L8 AND (PY<2004 OR AY<2004 OR PRY<2004)
     FILE 'REGISTRY' ENTERED AT 14:11:53 ON 26 JAN 2010
                 EXP ROSCOVITINE/CN
L10
               1 S E2-E3
     FILE 'HCAPLUS' ENTERED AT 14:12:12 ON 26 JAN 2010
            600 S L10
L11
=> s 15
L12
             80 L5
=> s 111 and 112
              3 L11 AND L12
=> d 113 1-3 ti abs bib
L13 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN
     Compositions and methods using Stat3 pathway inhibitors or cancer stem
     cell inhibitors for combination cancer treatment
AB
     The present invention relates to the composition and methods of use of Stat3
     pathway inhibitors or cancer stem cell inhibitors in combination treatment
     of cancer.
ΑN
     2009:332545 HCAPLUS <<LOGINID::20100126>>
DN
     150:345478
     Compositions and methods using Stat3 pathway inhibitors or cancer stem
TΙ
     cell inhibitors for combination cancer treatment
     Li, Chiang Jia; Mikule, Keith; Li, Youzhi
ΤN
     Boston Biomedical, Inc., USA
PA
SO
     PCT Int. Appl., 81pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 3
     PATENT NO.
                          KIND
                                   DATE APPLICATION NO. DATE
     _____
                           ____
                                   _____
                                                ______
     WO 2009036101
                           A1 20090319 WO 2008-US75906 20080910
PΤ
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              AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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PRAI US 2007-971144P P 20070910 US 2007-13372P P 20071213

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L13 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Antiproliferative effects of sapacitabine (CYC682), a novel 2'-deoxycytidine-derivative, in human cancer cells
- AΒ This study assessed the antiproliferative activity of sapacitabine (CYC682, CS-682) in a panel of 10 human cancer cell lines with varying degrees of resistance or sensitivity to the commonly used nucleoside analogs ara-C and gemcitabine. Growth inhibition studies using sapacitabine and CNDAC were performed in the panel of cell lines and compared with both nucleoside analogs and other anticancer compds. including oxaliplatin, doxorubicin, docetaxel and seliciclib. Sapacitabine displayed antiproliferative activity across a range of concns. in a variety of cell lines, including those shown to be resistant to several anticancer drugs. Sapacitabine is biotransformed by plasma, gut and liver amidases into CNDAC and causes cell cycle arrest predominantly in the G2/M phase. No clear correlation was observed between sensitivity to sapacitabine and the expression of critical factors involved in resistance to nucleoside analogs such as deoxycytidine kinase (dCK), human equilibrative nucleoside transporter 1, cytosolic 5'-nucleotidase and DNA polymerase-  $\alpha$ . However, sapacitabine showed cytotoxic activity against dCK-deficient L1210 cells indicating that in some cells, a dCK-independent mechanism of action may be involved. In addition, sapacitabine showed a synergistic effect when combined with gemcitabine and sequence-specific synergy with doxorubicin and oxaliplatin. Sapacitabine is therefore a good candidate for further evaluation in combination with currently used anticancer agents in tumor types with unmet needs.
- AN 2007:959718 HCAPLUS <<LOGINID::20100126>>
- DN 148:92336
- TI Antiproliferative effects of sapacitabine (CYC682), a novel 2'-deoxycytidine-derivative, in human cancer cells
- AU Serova, M.; Galmarini, C. M.; Ghoul, A.; Benhadji, K.; Green, S. R.; Chiao, J.; Faivre, S.; Cvitkovic, E.; Le Tourneau, C.; Calvo, F.; Raymond, F.
- CS RayLab Department of Medical Oncology, Hopital Beaujon, Clichy, 92110, Fr.
- SO British Journal of Cancer (2007), 97(5), 628-636 CODEN: BJCAAI; ISSN: 0007-0920
- PB Nature Publishing Group
- DT Journal
- LA English
- OSC.G 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
- RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L13 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Combination of a CDK inhibitor and CS-682 or a metabolite thereof
- AB A first aspect of the invention relates to a combination comprising a CDK inhibitor and  $1-(2-C-cyano-2-dioxy-\beta-D-arabino-pentofuranosyl)-N4-palmitoyl cytosine, or a metabolite thereof. A second aspect of the invention relates to a pharmaceutical product comprising a CDK inhibitor and <math>1-(2-C-cyano-2-dioxy-\beta-D-arabino-pentofuranosyl)-N4-palmitoyl cytosine, or a metabolite thereof, as a combined preparation for simultaneous, sequential or sep. use in therapy. A third aspect of the invention relates to a method of treating a proliferative disorder, said method comprising simultaneously, sequentially or sep. administering a CDK inhibitor and <math>1-(2-C-cyano-2-dioxy-\beta-D-arabino-pentofuranosyl)-N4-$

```
2005:523291 HCAPLUS <<LOGINID::20100126>>
ΑN
DN
     143:48129
     Combination of a CDK inhibitor and CS-682 or a metabolite thereof
ΤI
     Green, Simon; Sleigh, Roger Neil
ΙN
PA
     Cyclacel Limited, UK
SO
     PCT Int. Appl., 27 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
                         KIND DATE
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     PATENT NO.
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     WO 2005053699
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         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
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                                20070524 JP 2006-542014 20041203
     JP 2007513132
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A 20031204
W 20041203
     US 20070270442
                                             US 2007-581585
                                                                       20070420
PRAI GB 2003-28180
     WO 2004-GB5081
                          W
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 7
              THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> d his
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     FILE 'REGISTRY' ENTERED AT 14:01:17 ON 26 JAN 2010
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                 EXP 1-(2-CYANO-2-DEOXY-/CN
                 EXP 1-(2-C-CYANO-2-DEOXY-/CN
                 STRUCTURE UPLOADED
L1
L2
               3 S L1
     FILE 'STNGUIDE' ENTERED AT 14:08:01 ON 26 JAN 2010
     FILE 'REGISTRY' ENTERED AT 14:09:43 ON 26 JAN 2010
L3
                 STRUCTURE UPLOADED
               3 S L3
L4
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1.5
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1.6
              61 S L5/THU
L7
         974388 S CANCER OR TUMOR OR NEOPLA?
              49 S L6 AND L7
1.8
L9
              22 S L8 AND (PY<2004 OR AY<2004 OR PRY<2004)
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palmitoyl cytosine, or a metabolite thereof, to a subject.

FILE 'REGISTRY' ENTERED AT 14:11:53 ON 26 JAN 2010

EXP ROSCOVITINE/CN

L10 1 S E2-E3

FILE 'HCAPLUS' ENTERED AT 14:12:12 ON 26 JAN 2010

L11 600 S L10 L12 80 S L5

L13 3 S L11 AND L12

=> log hold

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 12.21 350.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE -2.55 -21.25

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:12:40 ON 26 JAN 2010

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:SSPTAEXO1623

PASSWORD:

\* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \* \* \* SESSION RESUMED IN FILE 'HCAPLUS' AT 14:13:21 ON 26 JAN 2010 FILE 'HCAPLUS' ENTERED AT 14:13:21 ON 26 JAN 2010 COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 12.21 350.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION
-2.55 -21.25

=> s CDK or (cyclin dependent kinase)

6706 CDK

43132 CYCLIN

1266568 DEPENDENT

370848 KINASE

27042 CYCLIN DEPENDENT KINASE

(CYCLIN(W) DEPENDENT(W) KINASE)

L14 29053 CDK OR (CYCLIN DEPENDENT KINASE)

=> s 112 and 114

L15 3 L12 AND L14

=> s 115 not 113

L16 2 L15 NOT L13

- L16 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Ataxia-telangiectasia and Rad3-related and DNA-dependent protein kinase cooperate in G2 checkpoint activation by the DNA strand-breaking nucleoside analogue 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabino-pentofuranosylcytosine
- $2'-C-Cyano-2'-deoxy-1-\beta-D-arabino-pentofuranosylcytosine$  (CNDAC), the AB prodrug (sapacitabine) of which is in clin. trials, has the novel mechanism of action of causing single-strand breaks after incorporating into DNA. Cells respond to this unique lesion by activating the G2 checkpoint, affected by the Chk1-Cdc25C-cyclin-dependent kinase 1/cyclin B pathway. This study aims at defining DNA damage checkpoint sensors that activate this response to CNDAC, particularly focusing on the major phosphatidylinositol 3-kinase-like protein kinase family proteins. First, fibroblasts, deficient in ataxia-telangiectasia mutated (ATM), transfected with empty vector or repleted with ATM, were arrested in G2 by CNDAC to similar extents, suggesting ATM is not required to activate the  $\bar{\text{G2}}$  checkpoint. Second, chromatin assocns. of RPA70 and RPA32, subunits of the ssDNA-binding protein, and the ataxia-telangiectasia and Rad3-related (ATR) substrate Rad17 and its phosphorylated form were increased on CNDAC exposure, suggesting activation of ATR kinase. The G2 checkpoint was abrogated due to depletion of ATR by small interfering RNA, and impaired in ATR-Seckel cells, indicating participation of ATR in this G2 checkpoint pathway. Third, the G2 checkpoint was more stringent in glioma cells with wild-type DNA-dependent protein kinase catalytic subunit (DNA-PKcs) than those with mutant DNA-PKcs, as shown by mitotic index counting. CNDAC-induced G2 arrest was abrogated by specific DNA-PKcs inhibitors or small interfering RNA knockdown in ML-1 and/or HeLa cells. Finally, two phosphatidylinositol 3-kinase-like protein kinase inhibitors, caffeine and wortmannin, abolished the CNDAC-induced G2 checkpoint in a spectrum of cell lines. Together, our data showed that ATR and DNA-PK cooperate in CNDAC-induced activation of the G2 checkpoint pathway. [Mol Cancer Ther 2008;7(1):133-42].
- AN 2008:64824 HCAPLUS <<LOGINID::20100126>>
- DN 148:322141
- TI Ataxia-telangiectasia and Rad3-related and DNA-dependent protein kinase cooperate in G2 checkpoint activation by the DNA strand-breaking nucleoside analogue 2'-C-cyano-2'-deoxy-1- $\beta$ -D-arabino-pentofuranosylcytosine
- AU Liu, Xiaojun; Matsuda, Akira; Plunkett, William
- CS Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
- SO Molecular Cancer Therapeutics (2008), 7(1), 133-142 CODEN: MCTOCF; ISSN: 1535-7163
- PB American Association for Cancer Research
- DT Journal
- LA English
- OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
- RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L16 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2010 ACS on STN
- TI Methods for enhancing antibody-induced cell lysis and treating cancer
- AB The invention relates to methods and products for treating cancer. In particular the invention relates to combinations of nucleic acids and antibodies for the treatment and prevention of cancer. The invention also relates to diagnostic methods for screening cancer cells.
- AN 2001:935435 HCAPLUS <<LOGINID::20100126>>
- DN 136:84677

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TI Methods for enhancing antibody-induced cell lysis and treating cancer
```

IN Weiner, George; Hartmann, Gunther

PA University of Iowa Research Foundation, USA

SO PCT Int. Appl., 312 pp.

CODEN: PIXXD2

DT Patent LA English FAN.CNT 1

FAN.	FAN.CNT 1 PATENT NO.						KIND		DATE		APPLICATION NO.							DATE			
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OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT